REMARKS

Status of the claims

Claims 1-4 are pending in the application, with claims 1 and 2 being amended herein and claims 3 and 4 being withdrawn.

Rejections under 35 U.S.C.§102 (b)

Claim 1 has been rejected under 35 U.S.C.§102(b) as being anticipated by Mule et al. The disclosure in Mule et al. of exposing isolated LAK precursor cells to IL-2 is asserted to meet the steps recited in claim 1. Claim 1 has been amended to recite that LAK cells are induced with an extract from *Lentinus edodes* mycelium. As such, the invention of claim is distinguished from Mule et al. and withdrawal of the rejection is respectfully requested.

Rejections under 35 U.S.C.§103

Claims 1 and 2 have been rejected under 35 U.S.C.§103 as being as being obvious over Mule et al. combined with Yamamoto et al. The Examiner notes that claim 1 does not define the screening material as an extract of *Lentinus edodes* mycelium. However, the Examiner asserts that the disclosure in Yamamoto et al. that extracts of *Lentinus edodes* mycelium can induce NK cells makes it obvious to use the *Lentinus edodes* mycelium extract of Yamamoto et al. in the LAK screening assay of Mule et al. Applicants traverse this rejection and withdrawal thereof is respectfully requested.

The instant invention

The instant invention, as encompassed by claim1, is drawn to a method for determining whether an extract of *Lentinus edodes* mycelium *in vitro* has a LAK activity-enhancing effect suitable for a subject, by the steps of:

(a) isolating peripheral blood from the subject to prepare lymphocyte fractions,

(b) preparing a LAK-induced sample, by treating the lymphocyte fractions with the extract of *Lentinus edodes* mycelium, and preparing a control sample in the absence of the extract of *Lentinus edodes* mycelium, and

(c) measuring and comparing the LAK activity of the LAK-induced sample and the control sample to determine the *in vitro* LAK activity-enhancing effect of the extract of *Lentinus edodes* mycelium for the subject.

Claim 2 further defines how the *Lentinus edodes* mycelium extract is made. The present inventors have demonstrated for the first time, with the invention disclosed in the specification, that the *in vitro* LAK activity enhancing effect of a screening material is parallel to the effect seen *in vivo*. For example, the present specification states,

> the *in vivo* cytotoxicity, which is exerted by the directed administration of an antitumor or anticancer agent, especially a LAK activity enhancer containing the extract of *Lentinus edodes* mycelium, has a positive correlation with the cytotoxicity which is exerted when lymphocytes prepared from a subject are activated with the LAK activity enhancer. See page 6, line 23 through page 7, line 1.

This finding with the invention is further supported by the results reported in Example 2, which describes the positive correlation with the *in vitro* and *in vivo* LAK activity enhancing effect of the extract of *Lentinus edodes* mycelium. See Figure 1.

Unobviousness of the invention over Mule et al. combined with Yamamoto et al.

As noted above, the rejection over the combined teachings of Mule et al. and Yamamoto et al. is based on the position taken by the Examiner that the disclosure in Yamamoto et al. that extracts of *Lentinus edodes* mycelium can induce NK cells makes it obvious to use the *Lentinus edodes* mycelium extract of Yamamoto et al. in the LAK screening assay of Mule et al. However, the Examiner has failed to establish a *prima facie* obviousness rejection based on the reference teachings for the following scientific reasons.

Yamamoto et al. discloses only that the extract of the reference has an effect on activating NK cells. There is no disclosure in the reference regarding any effect on LAK cell activity. NK cells and LAK cells are different populations of lymphocytes. See for example, the first paragraph of page 7.7.1 of Mule et al., which states, "The cytotoxic cells consist of either natural killer (NK) cells, which manifest cytotoxic activity without prior stimulation by antigen or activation by lymphokine, or lymphocyte-activated killer (LAK) cells which require prior activation with IL-2." As such, the teachings in Yamamoto et al. regarding NK cells do not provide motivation regarding LAK cells. It is well known in the field of immunology, and further confirmed by the disclosure in Mule et al. itself, that NK cell and LAK cells are two distinct cell types with independent properties and activation pathways. As such, an activity seen with NK cells is in no way indicative of an activity with LAK cells.

The instant invention considers and discloses for the first time an effect of LAK activity by the extract of *Lentinus edodes* mycelium and further discloses for the first time that the extract can enhance both the *in vitro* and *in vivo* activity of LAK cells to the same extent. As such, the present invention is not obvious over the combined teachings of Mule et al. and Yamamoto et al. and withdrawal of the rejection is respectfully requested.

Claim 2 is further distinguished from the disclosure of the references by further defining the invention by the preparation method of the extract. The extract of claim 2 is prepared in a different manner than that of Yamamoto et al., in that with the invention of claim 2 the extract is not prepared by extraction with hot water, but by the recited steps of the claim.

In view of the above amendments and remarks, Applicant believes the pending application is in condition for allowance. If the Examiner has any questions concerning this application, the Examiner is requested to contact MaryAnne Armstrong, Reg. No. 40,069 at the telephone number of (703) 205-8000.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

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Respectfully submitted,

By _____

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